Amendments to the Specification:

On page 1, line 1 of the specification, please delete the title and substitute therefor:

Methods for Identifying Compounds that Antagonize CD40 Signaling

On page 5 of the specification, please delete the paragraph spanning lines 27 through 31 and substitute therefor:

B1

Figure 1 depicts the structure NEMO, with various regions highlighted; the amino acid sequence is shown in SEQ ID NO:2. The region from amino acid 217 through 419 is believed to bind CYLD; homodimerization is thought to be mediated by amino acids 217 through 264. Binding to NIK and TIP60 is believed to occur between amino acids 95 and 264, while binding to RIP and A20 is through amino acids 95 through 218. NEMO binds to 14.7K via amino acids 180 through 419; binding to IKK-1 and IKK-2 is mediated by amino acids 44 through 86. The majority of mutations that result in familial IP are deletions of exons 3 through 10. The stippled regions labeled 'αH' are alpha-helical regions 'LZ' represents the leucine zipper region, and 'ZF' denotes the zinc finger. Amino acids 397, 400, 413 and 417 are believed to coordinate zinc.

On page 10 of the specification, please delete the paragraph spanning lines 19 through 28 and substitute therefor:

B2

NEMO and/or CYLD peptides that are useful in the inventive methods (including fragments such as those mentioned previously) may be expressed as fusion proteins with tag peptides that facilitate detection and/or purification. Such peptides include, for example, poly-His or the antigenic identification peptides described in U.S. Patent No. 5,011,912 and in Hopp et al., *Bio/Technology* 6:1204, 1988. Additional, useful tag proteins include green fluorescent protein (GFP; Chalfie et al., *Science* 263:802, 1994), an N-terminal peptide that contains recognition sites for a monoclonal antibody, a specific endopeptidase, and a site-specific protein kinase (PKA; Blanar and Rutter, *Science* 256:1014, 1992), birA (Altman et al., *Science*

B2

274:94, 1996)~~,~~ and glutathione S transferase (GST: Smith and Johnson, *Gene* 67:31, 1988).

On page 13 of the specification, please delete the paragraph spanning lines 11 through 23 and substitute therefor:

B3

One such assay is based on fluorescence resonance energy transfer (FRET; for example, HTRF®, Packard BioScience Company, Meriden, CT; LANCE™, PerkinElmer LifeSciences, Wallac Oy., Turku, Finland) between two fluorescent labels, an energy donating long-lived chelate label and a short-lived organic acceptor. The energy transfer occurs when the two labels are brought in close proximity via the molecular interaction between NEMO and ~~CLD~~ CYLD. In a FRET assay for detecting inhibition of the binding of NEMO and CYLD, europium chelate or cryptate labeled NEMO or CYLD serves as an energy donor and streptavidin-labeled allophycocyanin (APC) bound to the appropriate binding partner (i.e., CYLD if NEMO is labeled, or NEMO if CYLD is labeled) serves as an energy acceptor. Once NEMO binds CYLD, the donor and acceptor molecules are brought in close proximity, and energy transfer occurs, generating a fluorescent signal at 665 nm. Antagonists of the interaction of NEMO and CYLD will thus inhibit the fluorescent signal, whereas agonists of this interaction would enhance it.

In the specification, please delete the paragraph spanning line 32 of page 15 through line 4 of page 16, and substitute therefor:

B4

The database may be stand-alone, or the records therein may be related to other databases (a relational database). Examples of other databases include publicly available, well-known databases such as GenBank for peptides and nucleic acids (and associated databases maintained by the National Center for Biotechnology Information or NCBI), and the databases available ~~through www.chemfinder.com~~ on the World-Wide Web (www) through ChemFinder, a commercial (.com) portal of free and subscription scientific databases, or The Dialog Corporation (Cary, North Carolina) for chemical compounds.

In the specification, please delete the paragraph spanning line 29 of page 9 through line 9 of page 10, and substitute therefor:

B5

Also useful in the inventive methods are fragments of NEMO and/or CYLD. Particularly useful fragments of NEMO include the region from about amino acid 300 to 419, comprising a leucine zipper and zinc finger domain, and the region from about amino acid 387 to 419, comprising the zinc finger domain (see Figure 1); additional fragments thereof that bind CYLD can be identified as described herein, and will also be useful in the present methods. Such fragments include those that are truncated by about five to ten amino acids (i.e., fragments from x to y, wherein x is selected from the group consisting of 386, 385, 384, ~~3843~~ 383, 382, 381, 380, 379, 378 and 377, and y is selected from the group consisting of 409, 410, 411, 412, 413, 414, 415, 416, 417, 418 and 419, and in particular, 418 and 419), and those having an N-terminus between amino acid 300 and 387 (i.e., fragments from x to y, wherein x is an integer between 300 and 387, and y is selected from the group consisting of 409, 410, 411, 412, 413, 414, 415, 416, 417, 418 and 419). Particularly useful fragments of CYLD include those that are capable of binding NEMO.